

U.S. App. No.: 09/978,261  
Filed: October 15, 2001

### **REMARKS**

Claims 40 - 52 are currently pending and under examination. Claims 40 - 52 stand rejected. By this Amendment, claims 40 and 47 have been amended. Accordingly, upon entry of this Amendment, claims 40 - 52, as amended, will be pending and under examination. Claims 40 and 47 are independent.

Claims 40 and 47 have been amended to include detection "of an increase in the signal". Support for this amendment may be found *inter alia* in the subject application, as originally-filed, at page 63, lines 13 through 15.

Claim 47 has also been amended to include "and subsequent primer extension" in step (a). Support for this amendment may be found *inter alia* in the subject application, as originally-filed, at page 63, lines 13 through 15.

### **Double Patenting Rejection**

On page 22 of the March 3, 2005 Office Action claims 40-52 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1, 2, 5-9, and 43-52 of copending Application No. 10/719,480. The Examiner acknowledged that the conflicting claims were not identical but alleged that they were not patentably distinct from each other.

In response, in an attempt to advance the prosecution of the subject application, but without conceding either the correctness of the Examiner's position or the need to file a Terminal Disclaimer, Applicants enclose herewith a Terminal Disclaimer with respect to copending Application No. 10/719,480 and in accordance with 37 C.F.R. 1.321(c).

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Accordingly, Applicants respectfully request that this rejection be withdrawn.

**Rejection Under 35 U.S.C. § 102(b)**

Page 2 of the March 3, 2005 Office Action states that claims 47, 48, 51 and 52 are rejected under U.S.C. §102(b), as anticipated by Wang et al., (US Patent No. 5,567,583 ("Wang")). The Office Action includes responses to Applicants' arguments made in connection with these same rejections in Applicant's Response filed on December 1, 2004 to the June 3, 2004 Office Action.

The Office Action states that Wang discloses contacting the nucleic acid with an oligonucleotide primer pair comprising a first primer (i.e., the first primer taught by Wang) and a second primer (i.e., the oligonucleotide taught by Wang) under conditions that allow hybridization between complementary sequences in the target nucleic acid and the oligonucleotide primer pair. The Office Action also states that Wang discloses that the first primer and the oligonucleotide forms a triplex wherein the oligonucleotide indirectly binds to the strand of the target nucleic acid by the first primer.

Applicants respectfully disagree with the Office Action's rejections. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California* 814 F.2d 628, 631 (Fed Cir. 1987). Wang teaches the use of a blocking oligonucleotide which is designed to prevent primer extension of the bound primer. Therefore, even assuming the Wang primer/oligonucleotide pair binds to the target nucleic acid, primer extension will be prevented by the addition of the "bulky molecular moiety...at the vicinity of the 3' end to sterically hinder the polymerase from catalyzing the extension reaction." (column 5,

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lines 25 – 27). Without conceding either the correctness of the position stated in the Office Action or the need for amendment for patentability reasons, Applicants have amended claim 47 to include “and subsequent primer extension” in step (a). Therefore, amended claim 47 now recites that the target nucleic acid and the primer pair are contacted under conditions that allow hybridization between the target nucleic acid and the primer pair and subsequent primer extension. Accordingly, Wang does not anticipate claim 47 because Wang does not teach each and every element of the claim. Specifically, Wang does not teach the limitation of step (a) of claim 47.

Page 7 of the March 3, 2005 Office Action states that Wang discloses a moiety (i.e., the second fluorophore) capable of quenching, masking or inhibiting the activity of the signal generating moiety when located adjacent to, or in close proximity to the signal generating moiety (i.e., the first fluorophore) as recited in claim 47(a)(iii). The Office Action also states that Wang discloses that, when the first primer and the second primer are bound to one another, the signal (i.e., the signal generating moiety or the first fluorophore) is inhibited as recited in claim 47(a)(iii) wherein the acceptor fluorophore actually quenches that signal of the donor fluorophore.

However, Wang does not teach limitation (a)(ii)(B) (i.e., a moiety capable of quenching, masking or inhibiting the activity of the signal generating moiety when located adjacent to, or in close proximity to the signal generating moiety) or limitation (a)(iii) (i.e., when the first primer and the second primer are bound to one another, the signal is inhibited). The Office Action states that the acceptor fluorophore taught by Wang anticipates the “quenching moiety” limitation, however, Wang does not teach that the acceptor fluorophore actually quenches that signal of the donor fluorophore. Indeed, all of the examples in Wang disclose a donor:acceptor

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pair that displays a signal when in close proximity to each other and that the signal decreases upon amplification of the target nucleic acid (Example IV, column 12, lines 59 – 63; Figure 5). This is in direct contrast to the primer pair of the claimed invention. Claim 47(a)(iii) specifically states that “when the first primer and the second primer are bound to one another, the signal is inhibited.” Furthermore, a word search of the Wang reference failed to locate the terms: quenching, inhibiting or masking. Accordingly, Wang does not anticipate claim 47 because Wang does not teach each and every element of the claim. Specifically, Wang does not teach the limitation of steps (a)(ii)(B) and (a)(iii) of claim 47. Applicants respectfully request that this rejection is withdrawn.

Page 8 of the March 3, 2005 Office Action states that Wang discloses amplifying the target nucleic acid and separating the signal generating moiety and the quenching, masking or inhibiting moiety, thereby generating a signal, wherein detection thereof indicates the presence of the target nucleic acid in the sample as recited in claim 47(d). The Office Action also states that claim 47 does not require to detect signal increase.

Applicants respectfully maintain that Wang does not teach limitation (d) of claim 47 (i.e., amplifying the target nucleic acid and separating the signal generating moiety and the quenching, masking or inhibitory moiety, thereby generating a signal, wherein detection thereof indicates the presence of the target nucleic acid in the sample). Wang discloses a donor:acceptor pair that displays a signal when in close proximity to each other and whose signal decreases upon amplification of the target nucleic acid. Therefore, the end point measurement at the conclusion of the amplification process disclosed in Wang is exactly opposite what would be measured at the conclusion of the amplification process recited in claim 47.

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Without conceding either the correctness of the position stated in the Office Action or the need for amendment for patentability reasons, Applicants have amended claim 47 to include the positive limitation "detection of an increase in the signal". While performing the Wang method, one would have to measure a decrease in signal, which is inherently ambiguous and not as advantageous as measuring an increase in signal. The decrease in signal could mean that one has a positive result or it could indicate that the assay did not adequately perform. Accordingly, Wang does not anticipate claim 47 because Wang does not teach each and every element of the claim. Specifically, Wang does not teach the limitation of step (d) of claim 47.

Furthermore, Applicants maintain that it would not be obvious to one having ordinary skill in the art at the time the invention was made to perform the method recited in claim 47, in view of Wang.

For the reasons stated above, Applicants maintain that a the statutory requirements of a U.S.C. §102(b) rejection have not been met. Therefore, the 35 U.S.C. 102(b) rejection of claims 47, 48, 51 and 52 should be withdrawn and, accordingly, notice that claims 47, 48, 51 and 52 are in condition for allowance is requested.

**Rejections Under 35 U.S.C. § 103(a)**

Page 9 of the March 3, 2005 Office Action states that claims 40 - 42, 45 and 46 are rejected under U.S.C. §103(a), as unpatentable over Zhang et al. (US Patent No. 5,942,391 ("Zhang")) in view of Wang. The Office Action included responses to Applicants' arguments made in connection with these same rejections in Applicant's Response filed on December 1, 2004 to the June 3, 2004 Office Action.

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The Office Action states that the basis for the rejection is that claim 40 does not require an increase in the signal upon amplification of the target nucleic acid. Applicants respectfully disagree that it would have been obvious to perform the method recited in claim 40, in view of the patents of Zhang and Wang. However, without conceding either the correctness of the position stated in the Office Action or the need for amendment for patentability reasons, Applicants have amended claim 40 to include the positive limitation "detection of an increase in the signal". Therefore, in view of the addition of this positive limitation to claim 40, Applicants respectfully request that the 35 U.S.C. 103(a) rejections be withdrawn.

The Office Action also states that there is no evidence that a blocking oligonucleotide (i.e., said oligonucleotide) taught by Wang serves to compete with the second primer of Wang. Wang teaches the use of a blocking oligonucleotide which is designed to prevent primer extension of the bound primer. Therefore, even assuming the Wang primer/oligonucleotide pair binds to the target nucleic acid, primer extension will be prevented by the addition of the "bulky molecular moiety...at the vicinity of the 3' end to sterically hinder the polymerase from catalyzing the extension reaction." (column 5, lines 25 – 27). Accordingly, it would not have been obvious to perform the method of claim 40 in the presence of a blocking oligonucleotide, which would only serve to compete with the second primer of the primer pair of the subject invention (i.e., the primer comprising a moiety capable of quenching, masking or inhibiting) and thereby block primer extension. Therefore, it would not have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 40, in view of the patents of Zhang and Wang and the 35 U.S.C. 103(a) rejections should be withdrawn.

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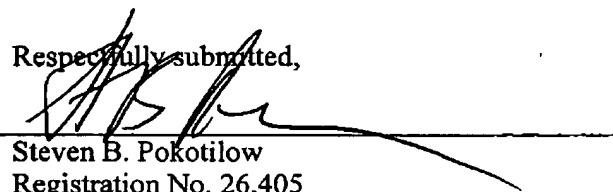
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Furthermore, the deficiencies discussed supra are not cured by the inclusion of Heller (US Patent No. 5,532,129) and Segev (US Patent No. 5,437,977) because neither Heller nor Segev, alone or in combination with Wang and Zhang discuss, suggest or teach the method of claim 40. Therefore, the 35 U.S.C. 103(a) rejections of dependent claims 41, 42, 45 and 46 should be withdrawn and a Notice of Allowance should be issued.

### CONCLUSION

Applicant respectfully submits that this application is in condition for allowance. Early and favorable action is earnestly solicited. No fee, except for the fee in connection with filing the Terminal Disclaimer, is believed due in connection with the filing of this Amendment. However, if any additional fees are due the amount of such fee may be charged to Deposit Account No. 19-4709.

Respectfully submitted,



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